AD NUMBER

AD837889

NEW LIMITATION CHANGE

TO

Approved for public release, distribution unlimited

FROM

Distribution authorized to U.S. Gov't. agencies and their contractors; Critical Technology; 01 JUL 1968. Other requests shall be referred to Department of the Army, Fort Detrick, MD 21701.

AUTHORITY

SMUFD D/A ltr, 22 Oct 1971

TRANSLATION NO. 500

DATE: 1 July 1968

DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

F. Henke & O. Lubarsch (Editors), Hdb. Spez. Path. Anat. u. Histol., Vol. I, Pathology Section, p. 84

500

Section 13: (From H. Schleussing: Meningitis (without the specific forms)

Anthrax bacillary meningitis.

The meningeal inflammation caused by the anthrax bacillus (Bacillus anthracis) was described by Wagner as early as 1874. A large number of individual observations were subsequently published and were collected in 1913 by Fulci. Infection usually occurs via the circulation, but the meninges may also be infected by the lymphatic route or by direct transmission from anthracic foci on the head, the throat and the upper respiratory and digestive tracts. Pathologic-anatomically, nearly all reported cases are dominated by extensive hemal extravasation in the meninges. It must be emphasized in opposition to reports to the contrary that this involves a genuine inflammation and not hemorrhages. The disorder usually localizes in the region of convexity and thus leads to the picture of the so-called red hood. Toxic injuries to the vascular walls must be considered instrumental in extensive hemal exudation (F. Herzog 1915, Bexi 1926 and others). Aside from hemorrhages by diapedesis, anthracic meningitis is marked also by necrosis and rupture of the larger vessels. Although the leucocytes may be dominated by erythrocytes, lymphocytes and histiocytes in a few cases, leucocytes with lobulated nuclei as a rule are present in copious amounts. The presence of large quantities of anthrax bacilli within the lymphatic sheaths of vessels has been pointed out from various quarters.

Vol. II, p. 734

Rarer Forms of Acute and Subacute Lymphadenitis. (From L. Jores)

Fibrinous exudation is frequently seen in pharyngeal diphtheria, in which leucocytic emigration takes place in the cervical lymph glands and networks of fibrinous threads are found in the sinuses, follicles and the blood vessels, the same is true of pneumonia. Necrotic foci (e.g. in typhus) may also be permeated with fibrin. Fibrinous - hemorrhagic inflammations also occur, most pronounced in the case of anthrax (lymph nodes are considerably enlarged), where the demonstration of massive bacilli usually succeeds; in addition, they are seen in glanders and plague.

Vol. III, pp. 803-820

(From W. Mohr: Rare Infectious Diseases)

Anthrax, Charbon bacteridien, Splenic-Fever.

Anthrax is an infectious disease with a predominantly septicemic course. It occurs principally in plant-eating mammals and swine. Human infections as a rule develop through contact with diseased animals or animal products.

History: Anthrax was known in ancient times as an animal affliction which occasionally reached epizootic proportions and was transmissible to humans. The anthrax bacillus was first seen by Pollender (1849) in the blood of anthracic animals and was cultivated artificially by Robert Koch in 1876. The latter also observed sporulation for the first time and discovered the epidemiology of anthrax based on the high resistance of the spores.

Etiology: The anthrax bacillus (B. anthracis) is a non-motile, gram-positive rod with square ends, 4 - 10 microns long. In the animal organism, the anthrax bacillus occurs as a single rod and is surrounded by a gelatinous envelope, the capsule. The question of toxin production by the anthrax bacillus as a cause of many symptoms of the disease is not clear. The concept of toxin production is contrasted with the assumption that capillary emboli due to massive propagation of anthrax bacilli are the cause of death. Anthrax bacilli die within 2 - 4 days in anaerobic putrefaction of unopened cadavers. The anthrax bacillus sporulates outside the animal organism in the presence of oxygen. Anthrax spores are extremely resistant. Still, they may be inactivated with hydrochloric acid, and this 9 - 10 times as rapidly as with sulfuric acid. They remain infective for 30 to 40 years in the dry state. The bacillus grows on the customary nutrient media with thread formation. Reproduction even takes place in the external world, provided sufficient nutrients and humidity are present, especially among anthrax germs excreted with the feces.

Transmission: Among human beings, infection as a rule emanates from the external skin. Intestinal anthrax is rare and occurs primarily in uncivilized countries after consumption of spores with the meat and milk of anthracic animals. Primary pulmonary anthrax occurs among rag sorters (wool-sorter's disease) and among peoples of the steppes. In the steppes, dried cattle excreta are used as fuel in the absence of other materials. In blowing on the fire, anthrax spores contained in the feces are inhaled. For this reason pulmonary anthrax is found in these regions predominantly among women.

Oral infection is the rule among mammals and birds developing exclusively through the agency of spores. Since no spores are produced in anthracic cadavers, carnivores will infect themselves during the consumption of such cadavers only when these are no more than 1 - 2 days old and the feeding animals have wounds in the oral cavity, the pharynx or the esophagus. On the other hand, spores are ingested by herbivores on the meadows along with their fodder. For this reason anthrax infections occur essentially among herbivores. They are most prevalent among cattle and sheep. Thus, anthrax among herbivores is not a contact infection, but a ground infection. Occasionally, blood-making insects

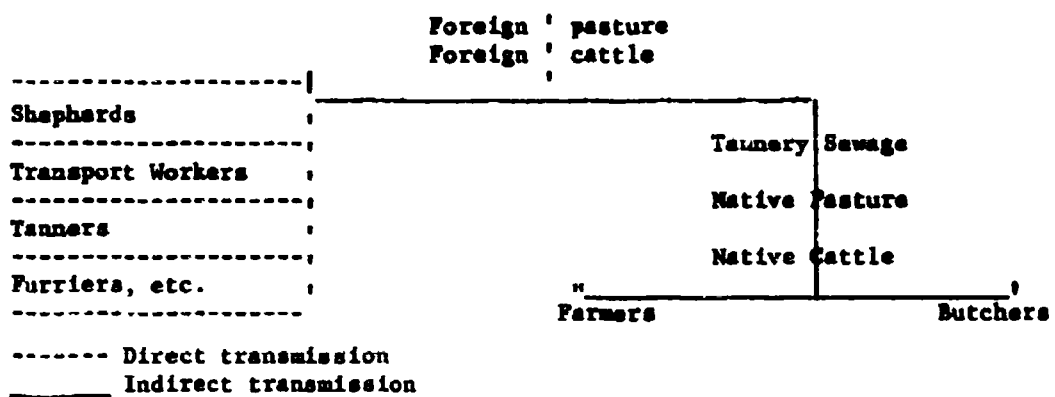
may contribute to the dissemination of anthrax.

Incidence: Anthrax has a world-wide distribution. In Europe with the exception of East and South-East Europe it is far rarer due to legally enforced controls. The high resistance and prolonged viability of anthrax spores impedes the eradication of this disease even in Europe. Moreover, additional infections are caused by importation of animal products from countries with a high incidence of anthrax. According to a compilation by Muesseneir, the testing of dry hides by Ascoli's method up to the year 1929 uncovered 79 (4%) positive hides among 1,952 from China, 59 (0.4%) among 12,533 from India, 231 (1.2%) of 18,705 from Argentina, 126 (2.1%) of 5,900 from Uruguay, 6 (2%) of 300 from Senegal, 69 (1.3%) of 5,152 from Mombassa and 55 (1.3%) positive hides among 4,100 from Abessinien just to mention the most important import countries. The role played by anthrax in some countries is reflected in the report by Delpy and Kaweh, who state that more than one (1) million sheep died of anthrax in Iran during 1944/45. In Germany, cessation of foreign imports during the first world war led to a considerable abatement of anthrax cases. A renewed rise was noted from 1918 to 1930, especially in Schleswig-Holstein, which occupies the first place in the incidence of anthrax in Germany. This is due to the large tanneries located here, which process foreign hides. Since 1932 the number of anthrax infections decreased and reached a low of 0 during the last world war, followed by a renewed rise to 10 in 1949. Still, this number is quite small compared to 408 cases among cattle and 1,014 among hogs in 1914. Until 1930, the river Stoer, on which Neumuenster, the principal North German leather processing center, is located, absorbed the wastes from tanneries without filtration. The number of animals lost due to anthrax decreased considerably upon the installation of a purification plant for tannery sewage in 1930.

Generally speaking, the conditions for the persistence of contamination on meadows and pastures are not favorable in German's climate, but anthrax may become endemic even here on moist terrains since the spores survive for the longest time on grounds that are moist or exposed to occasional floods.

Usually anthrax represents an imported infection and the chain of contagion is assumed to proceed according to the following pattern.

Infective chain of the anthrax bacillus according to Graf:



Anthrax in animals: Among ruminants and horses, anthrax usually occurs septicemically. The infection at times has a peracute course, but usually it is acute or subacute. Initially, great agitation sets in, accompanied by high fever. Consumption of fodder ceases. Hemorrhages from the intestine, the nose and mouth, as well as sanguinolent urine are frequently observed. The duration of disease is 1 - 3 days on the average. A chronic course leads to death in 2 - 3 months with severe emaciation. The abortive form frequently ends in recovery. The worst conspicuous anatomical changes in acute cases are incomplete rigor mortis, serous exudates and hemorrhages in all organs. The lymph nodes and, especially, the spleen are swollen. The splenic pulp is dark red and has a mushy consistency. The liver, kidneys and breast muscle are degenerated.

The pig usually acquires a local infection of the pharynx and the regional lymph node (anthrakic angina) which has a benign course. It is frequently found in apparently healthy swine processed in slaughter houses.

Human Anthrax: In Germany, this disease afflicts very definite occupational groups, according to Graf's compilation in the following sequence in decreasing frequency:

1. Stevedores
2. Tanners
3. Men and women in industries processing fur, hair, and wool, such as brush factories, horse hair, and thread spinning mills, wool combing establishments as well as enterprises processing rags.

Infections from finished products of animal origin, such as shaving brushes, brushes and wool clothing are rare.

4. Animal husbandmen
5. Butchers
6. Veterinarians

The mortality of group 1 amounted to 38.7% among 150 cases reported during 1910 - 1923, contrasted with a death rate of 13.4% of 476 cases among tanners. Groups 1 - 3 almost invariably contract sporal infections, whereas groups 4 - 6 usually reveal bacillary infections.

Thus, Hamburg with an average of 6.5 cases per one (1) million inhabitants, together with the District of Luneburg with 5.8 and Schleswig with 4.8 had the highest incidence compared to an average of 1.6 cases in the remaining parts of Germany. The situation gains in clarity with the statistics of the Guild of Leather Workers for the years 1910 - 1925, as reported by Graf. According to these data, cases of human anthrax originated in

Trade and transportation	147	times with 57 deaths = 39%
Tanneries	550	times with 73 deaths = 13%
Dealings with hair and its processing	350	times with 103 deaths = 29%
Agriculture and slaughtering	1,060	times with 106 deaths = 10%
On the average	2,107	times with 339 deaths = 16%

During the war of 1940 - 1945, the incidence of anthrax in transportation and tanning approached zero (Graf). There were no cases during 1943 - 1947, the next two were reported in 1948.

Table 1

The disease was incurred due to dealings	Number of anthrax cases during				
	1910-1929		1930-1937		1938
	Total	Per Year	Total	Per Year	Per Year
With living animals	31	2	13	2	9
With emergency slaughter	1,120	56	363	45	39
With expired animals	262	13	55	7	2
With animal hair or bristle	214	11	67	8	7
With hides or fur	896	45	141	18	24
Of other physical nature	51	3	32	4	3
Of non professional type or without statement of purpose	286	14	53	7	4
Total	2,860	144	724	91	88

This correlation with certain occupations is also reflected with exceptional clarity in the preceding Table 1 of the National Public Health Service for the years 1910 - 1938.

Valuable information is gleaned also from a compilation of the locations at which 946 infections occurred during 1906 - 1948. Work in the storehouses of tanneries was responsible for 159 cases with 24 fatal issues, occupation in water treatment shops caused 312 cases with 27 fatalities and work in lime treatment shops, 218 cases, of which 26 died.

These involved predominantly cutaneous anthrax. The infecting spores enter the organism through the skin, which usually is injured.

Due to the affinity of this infection for certain occupations, it is found among men at a rate exceeding 90%. Thus there was only one woman among eleven cases of cutaneous anthrax observed at the Tropical Disease Hospital during 1931-1939. Eight of these 10 men were employed in the harbor as transport or storehouse workers. The anthrax cases treated at the Hamburg Tropical Institute since 1949 involved stevedores (3 cases) who unloaded pelts from East Asia and Turkey, and nearly as frequently male (4) and female (6) workers of a wool carding plant who processed woolen material, primarily goat hair, usually from Australia and South Africa.

Pathological Anatomy: A carbuncle develops at the site at which anthrax bacilli enter the skin or mucous membrane. It shows a central-neurotic eschar with surrounding coarse tissue infiltration. Copious cells permeate the connective tissue in this region, frequently even hemal extravasates and deposits of fibrin. The eschar consists of necrotic skin tissue and destroyed epithelial cells. Anthrax bacilli contained therein usually have died or are demonstrable only in small numbers; however, there are copious pyogenic bacteria, predominantly streptococci. Viable bacteria are found principally in the edematously saturated surroundings of the carbuncle.

Anthrax edema also develops in the region where bacilli have penetrated the skin. The result is a cellular-serous saturation of the skin and the subcutaneous connective tissue. In some cases these infiltrates may be sanguinolent, and gangrene may develop in circumscribed places.

Pulmonary anthrax, whose pathologic-anatomical lesions were studied in detail by Eppinger, frequently reveals hemorrhagic infiltrates and pustules in the nasal mucous membrane. The diffusely erythematous laryngeal mucous membrane also shows such changes. The lungs are severely hyperemic. The initially lobular pneumonic infiltrates have a tendency to confluence and the formation of lobar infiltrates. In addition, there may be sanguineous infarcts and occasional frankly gangrenous foci. Very often the pulmonary disorder is accompanied by exudative pleuritis. The trunk bronchi occasionally show the development of anthracic, fibrinous pseudomembranes (E. Fraenkel and Heye). The bronchial glands are always highly swollen, hyperemic and permeated with hemorrhages. Consequently they may at times appear to be dark red, almost black.

The spleen is soft, rich in blood and usually enlarged. There is a certain divergence here from findings in animals, whose organ, although enlarged, is very brittle and reddish-black (on which circumstances the designation "splenic fever" is based).

The kidneys are filled with blood and show partial epithelial degeneration. The observation that the glomerular vessels are very frequently filled with bacilli, seems significant.

The brain and the meninges are edematous and hyperemic. Hemorrhages of varying size are not at all rare. These may also be transformed into foci of softening.

Nearly all cases of internal anthrax and anthracic sepsis reveal such changes. At times, such a hemorrhage may encompass the brain in the form of a hood.

Similarly to the cutaneous lesions, circumscript, carbuncular infiltrations or flower bed-like elevations are found in cases of intestinal anthrax, rarely in the stomach, more often in the duodenum, most frequently in the small intestine and colon, seldom in the rectum (in contrast to amebic dysentery). These consist of serous-purulent infiltrations in the submucosa. The mucous membrane above such infiltrates undergoes a gradual stretching process ending in ulceration. The surroundings of these ulcers is gelatinous. The number of foci in the intestinal mucous membrane may be considerable, 40 or more. The mucous membrane between these points usually is quite red and slightly gelatinous. More profuse hemorrhages may occur in the onward course of the disease. Almost invariably the infection metastasizes to the mesenteric lymph glands, at times to the retroperitoneal ones which then in turn swell and reveal heavy cellular infiltration, frequently marked by a dark red appearance due to hemorrhages.

Clinic and course: Four human forms are recognized:

1. Cutaneous anthrax. 95% of all cases,
2. Anthracic edema, which usually follow cutaneous anthrax,
3. Pulmonary anthrax (wool-sorter's disease),
4. Anthrax of the gastrointestinal tract.

Table 2 reproduced below after Graf offers a perspective on the distribution of the individual disease forms among 682 cases reported in Germany during 1931-1938.

Table 2

Seat of infection	Total	Fatalities	Mortality Percent
Internal anthrax	17	17	100
External anthrax			
Head	124	13	10.5
Throat and neck	98	26	26.5
Arm	419	22	5.3
Elsewhere	24	3	12.5
Total	682	81	11.9

1. Cutaneous anthrax. Incubation time. About 2 -3 days after infection, very rarely after only a few hours, a reddish area about the size of a penny appears containing in its center a slightly raised spot resembling a flea bite. The latter changes to a small papule and very soon reveals a bluish-black, hard center. The initial state of infection rarely comes under medical observation; this usually occurs after formation of the carbuncle. The primary focus is found predominantly in early accessible regions of the skin, such as the hands, arms, or the face. In most cases there is only one focus, but several may also appear. In that case it invariably involves auto-infection. After 12 to 15 hours, heavy redness and swelling appears around the papules. The papule changes into a vesicle with a yellowish or sanguine and purulent content. The drying vesicle or scratching on the part of the patient leads to the formation of a dark bluish-red or black eschar which expands in depth and width. Together with the densely infiltrated surrounding, it forms a course node, the carbuncle. New vesicles may erupt on the edge of the eschar. The eschar rapidly turns black, dry and very firm ("hard as shoe leather"), it continues to expand in width and depth, and extensive edema may set in in the proximity, disfiguring the affected part. Proceeding from the carbuncle, inflammatory processes lead at an early stage along the lymph vessels to the regional lymph nodes. These may be very painful in contrast to the carbuncle which usually is painless and insensitive. Jourdan, in a report of 10 cases from the region of Arles (southern France) pointed out in 1947 that only two of these showed a typical pustula maligna, whereas 8 persons revealed hemorrhagic vesicles that developed an eschar after a few days. This was generally followed by the development of additional vesicles, nearly always with very pronounced lymphangitis. He noted a mixed infection with tetanus bacilli, in which the anthracic disorder was cured by serum treatment, while the tetanus infection remained intractable and led to death.

The end of the first week of illness or the second week brings suppurative demarcation around the necrotic tissue. At the same time the edema retracts, the eschar softens and loosens, the lymphatic inflammation abates. A granulating surface remains, which later turns to a scar.

The whole process is accompanied by early appearance of such general symptoms as fever, exhaustion, and inappetence. Severe cases may involve intensified manifestations on the first few days, including pain in the head and limbs, septic temperatures and circulatory insufficiency. The situation may be rendered more difficult by sanguineous vomiting and bloody diarrhea, profuse sweating, cyanosis, collapse temperature and cessation of intestinal secretion (similar to asphyctic cholera). In most cases death occurs at the end of the first week or the beginning of the second.

It is obvious from the preceding discussion that the location of the pustula maligna is of great importance to the total course of the condition. Graf did not find a single fatality among patients with pustules on the trunk and on the limbs. Of 20 cases with carbuncle localization on the forehead, neck and eyes, 1 terminated in death; there were 15 fatalities among 55 of his patients with lesions in the face or on the shaved throat. The removal of the fatty layer that under normal conditions protects the skin, and the frequent development of small cutaneous defects due to shaving certainly play an important role in the infecting process. Graf found 29 patients with pustules on the throat, of whom 12 died.

2. Anthrax edema is situated predominantly on the face and in the mucous membranes. The swelling is doughy, soft and translucent with a light red to dark red or even anemic appearence. The skin, partially smooth and partially areolate, frequently is marked by vesicles that may burst and dry into scabs. In that case there is no divergence from the carbuncle. A strict differentiation of these two initial forms is impossible in many cases. According to earlier authors, the process of edema usually is more severe and unfavorable prognostically. Localization in the mouth or in the region of the upper respiratory tract is particularly dangerous, since there is a possibility of interference with breathing and swallowing, as well as the danger of an ascending infection.

Even meningitic conditions are seen occasionally. These cases are relatively rare, however; only 10 had been listed in the world literature until 1947. Since then, three additional cases were reported by Claisse and Pestel, Shanaham, Griffin and V. Auersperg, as well as by Eck. Claisse and Pestel's case involved a 45-year-old dock worker who had unloaded goat skins from Yugoslavia and who shortly thereafter developed a furunculoid ulcer in the neck, which remained unnoticed for some time. A severe comatous situation developed within 28 hours, leading to death with the appearance of numerous petechial hemorrhages on the whole trunk. Copious anthrax germs were demonstrated in the liquor preparation and in the culture.

Shanaham, Griffin, and V. Auersperg observed a vesicular eruption on the upper lip of a 57-year-old cotton picker. Culture of the vesicular content yielded anthrax bacilli. A meningitic condition developed as early as the second day of illness. Anthrax pathogens were found also in the liquor culture. The patient was saved by treatment commencing the second day, consisting of

large doses of penicillin (110,000 on the second day, 4,400,000 on the third, partly intrathecally) and anthrax serum as well as sulfadiazin.

The last case, described by Eck in 1949, involved a 1-year-old girl who suddenly became ill with a clinically mysterious symptomatology. Section revealed hemorrhagic leptomeningitis caused by anthrax bacilli. The pathogen originated in the stuffing of a toy dog with which the child had played. No cutaneous pustule was demonstrated in this case.

3. Pulmonary anthrax (wool-sorter's disease) usually commences suddenly with rigor and fever. The general manifestations mentioned above appear early and are accompanied by symptoms of the respiratory passages, such as dyspnea, erythema and swelling of the nasal, pharyngeal and laryngeal mucous membranes. This disorder is nearly always acquired by aspiration of spore-containing dust, as during the sorting of wastes and rags or in wool carding mills (such a case was recently observed in Hamburg). The initial picture of bronchitis was followed by advancing dyspnea and developed into a pneumonic infiltrate with foamy-sanguineous expectoration. Pleuritic exudate frequently is an additional factor. Bacilli are demonstrable in the sputum. Death occurs on the 2nd or 3rd day, spontaneous cures are very rare. According to a compilation by Lommel, there were 108 fatalities among 113 cases of pulmonary and intestinal anthrax.

4. Anthrax of the gastro-intestinal tract shows the general symptoms listed above combined with violent vomiting often with sanguineous admixtures, diarrhea with purely watery-serous stools, occasionally even streaked with blood. This infection is contracted by consumption of contaminated meat or milk. While the bacilli are inactivated in the acid gastric juice, the spores remain viable and germinate in the small intestine. They subsequently lead to multiple carbuncles of the mucous membrane and a septic spleen. The abdomen is very sensitive to pressure and shows meteoristic distension at an early stage. The violent course is usually followed by death on the 2nd or 3rd day, offering the appearance of peritonitic or toxic collapse. More benign cases are observed among larger groups of people partaking of infected food. The prognosis of intestinal anthrax generally is no more unfavorable than that of the cutaneous carbuncle.

The individual pictures cannot always be differentiated with such clarity according to their primary localization. Primary anthrax of the internal organs may produce cutaneous metastases. Pulmonary anthrax may lead to intestinal manifestations. Secondary intestinal infections may also develop by transport of bacilli from a carbuncle. The various localizations all share the general manifestations of severe infection, those of anthracic sepsis. These septic signs are quite rarely observed without a distinct primary localization. This probably involves the acquisition of the pathogen through the lungs or the upper air passages.

Diagnosis. The diagnosis of cutaneous anthrax usually is quite uncomplicated. It is readily delineated against the simple carbuncle, which is very painful and slower in developing, and which later discharges copious pus from several cutaneous openings. Glanderous nodes can be differentiated from anthrax by its very numerous cutaneous nodules and ulcers. Compared to erysipelas, anthrax edema does not show as distinct a delimitation against healthy skin.

Confusion with erysipelas is possible especially in the region of the eyelids, largely in the case of anthrax edema. Bacteriological examination is an indispensable aid in the confirmation of anthrax and must be resorted to in every case. Often the examination of the secretion taken from the focus of infection suffices for microscopic identification, at times anthrax bacilli are present in very small numbers or mixed with other bacteria, necessitating an animal test or a culture. When the suspected material is instilled subcutaneously in mice or guinea pigs, the anthrax bacilli multiply at an extraordinary rate and induce fatal sepsis. They are then readily demonstrable in the blood. Cultural studies are made on agar surface cultures (colonies resembling Medusa's head) and gelatin plates.

The identification of anthrax of the gastro-intestinal tract is more difficult. The anamnesis may offer important clues, if consumption of the meat of anthracic animals has been admitted.

Pulmonary anthrax may initially be confused with croupous pneumonia. In such cases the examination of sputum and especially, of blood cultures, offers important information. Blood cultures are best grown on dextrose broth or dextrose agar. In the case of massive bacillary invasion of the blood, as seen in the last stages of the disease, the pathogen becomes visible on blood slides. Staeubli tested a direct method of demonstration by drawing a fresh drop of blood from an injection point, diluting it with a 10 - 15-fold amount of 3% acetic acid, centrifuging the mixture, and then staining the sediment, consisting of leucocytic nuclei and pathogens, with May-Gruenwald. The liquor may also contain large amounts of anthrax bacilli. In addition, anthrax bacilli may be demonstrated in the bone marrow.

In addition to bacterioscopic and cultural tests and the animal experiment, veterinary medicine makes use of the thermoprecipitation after Ascoli. The suspected material (blood or splenic juice) is diluted with physiological saline. The mixture is then boiled for a few minutes and filtered. The customary specific anthrax serum is added to the cooled clear filtrate.

Prognosis. Cutaneous anthrax has the most favorable prognosis. Ninety percent of all cases are restored to health occasionally without any kind of treatment. A case of external anthrax that is recognized and treated early, is nearly always curable. The prognosis deteriorates upon the appearance of general infective manifestations. Anthracic edema is generally considered to be less favorable prognostically than the carbuncle. Even intestional anthrax may be cured, but the danger of general infection is greater here. Pulmonary anthrax justifies the most inauspicious prognosis. The rate of fatal terminations lies between 50 and 87%, according to some authors even near 100%. Blood cultures figure conspicuously in the evaluation of the prognosis in these last two forms: If numerous colonies grow out the prognosis is very doubtful; if only a few appear, a favorable outcome may still be hoped for. Recovery usually produces a prolonged immunity.

Therapy. Surgical treatment of anthrax pustules has fallen into general disrepute; considering the experience gained during the past years, it may now be considered a virtual blunder. Conservative therapy of the anthrax carbuncle occupies the foreground, being based on the assumption that carbuncle

formation represents a defensive measure on the part of the organism which appears only in more resistant individuals and therefore permits a more favorable prognosis than a diffusely commencing symptomatology. Scholl, who compared surgical and conservative approaches, found 44% fatalities connected with the former, and 7% with the latter. Treatment will therefore be limited to cleansing of the pustule's surroundings, immobilization and elevation of the affected limb in the event the pustules are located on the arm or the leg, and protection of the pustules with a salve dressing, e.g. penicillin or sulfonamide salve.

Local application of heat in the form of shortwaves, irradiation with heat-giving lamps and cataplasms is also being recommended. Such hyperemization is expected to exert a salutary influence on the healing process. Gruber and Futtaki observed anthracocidal substances in the obstructed lymph of rabbits. This seems to suggest occasional employment of Bier's method in human medicine, when the affection is localized in a suitable area. This method of blockage was also recommended by Zuelzer; it may conceivably impede the dissemination of bacilli via the lymph passages.

However, it must be remembered in connection with all methods of treating cutaneous anthrax, that the number of spontaneous cures is very large, and that the therapeutic value of these methods must not be overrated.

Many different remedies have been utilized in the treatment of anthrax. Thus, Becker recommended a single dose of 0.6 neosalvarsan. Gilbert (Northern Rhodesia) also treated 9 patients with neosalvarsan, 7 of whom showed remarkable improvement after one injection, although 2 required large doses. Scalari confirmed this success in 5 cases. Spencer successfully employed arsenic preparations in the treatment of a group infection caused by consumption of meat from a diseased animal. On the other hand, Graf considers management with silver and arsenic preparations to be inefficacious on the basis of his extensive experience (Baumann had recommended agrochrom).

The introduction of serum therapy brought a very considerable therapeutic advance, carried out in human medicine in the form of passive immunization according to Scalvo's method, who in 1903 reported on the first 164 cases successfully treated with serum. The employment of this method lowered the mortality from 24% to 6%. A report from England involving 800 cases claims a drop in the death rate from 48.3% to 4%. In Argentina, Penna observed a mortality of 10% with serum therapy; Andrew, in Bulgaria, one of 4.2% contrasted with 25% prior to serum therapy.

It is imperative that treatment be commenced as early as possible. High initial dosages of 50 - 500 cm^3 are recommended. Application generally may be intramuscular. Advanced cases requiring rapid efficacy may be treated intravenously (Cuckeli and others).

The serum is obtained from horses, cattle, sheep, donkeys, and mules. Bovine serum offers the advantage of causing serum disease less frequently than equine serum. Serum is produced by various methods, but no important difference in the efficacy of the several methods is evident. According to Sobernheim, the serum produced by Merck and the Hoechster Farbwerke is generally

used in Germany. The nature of serum activity is not clear. Although various antibodies have been demonstrated in high quality sera, several authors do not credit them with a decisive role in the activity of the serum. This is usually attributed to the anti-infectious sera. However, it has no bactericidal or phagocytosis-promoting substances. Patterson assumes that negative-chemotactically active substances are formed during infection, whose inhibitory effect neutralized the antibodies contained in the immune serum and thus clears the path for phagocytosis.

Combined therapy has also been tired. Hodgson used serum in conjunction with a neosalvarsan preparation and Bierbaum had previously added salvarsan to serum therapy. The investigators claimed very good results for such mixed treatment, provided it is dispensed early.

There also has been some opposition to serum therapy. Thus, Roggeri does not believe this treatment influenced his 362 anthrax cases decisively. The same tendency seems evident in the results of experimental work done by McCullough and V. Auersperg in 1947. The writers infected mice, guinea pigs and rabbits with an anthrax broth culture and treated them with penicillin and anthrax serum. While penicillin was able to protect the animals, the antiserum proved useless and was found to be toxic in blank tests. Schmidt (Marburg) also rejects serum therapy, since in his opinion the protein-containing capsule formed by the pathogen in the human organism prevents the activity of instilled antibodies. Autohemotherapy has also been described as successful. Erb performed hemal blockage after Laewen with peripheral injection of the carbuncle.

Sulfonamides have also been used in anthrax and proved to have some efficacy. J. Doerffel was the first to successfully resort to sulfonamides in the form of Prontosil rubrum in the treatment of anthrax. He was followed in 1941 by Bergmann with a report on 2 cases. In Hungary, Ferenci published a detailed account of successful therapy with para-amidobenzol sulfamide (Deseptyl). The preparation was dispensed per os and as an injection. V. Brede and Nagy achieved good results with 2 - p - aminobenzolsulfamido - 4 - methylthiazol in 11 cases of cutaneous anthrax. Their patients included four who had previously undergone ineffectual serum therapy and had reached a very serious condition. Schoenfeld and Kimmig, on the other hand, warn against unduly high dosages of this drug due to the danger of venal damage (crystallization in the venal canaliculi) and neuritides. Recently, the compound sulfadiazine (Pyrimal and Debenal in the German nomenclature) has been successfully introduced into anthrax therapy, especially in America. The reports of Lebrun, Shanahan, Griffin, and V. Auersperg, as well as Reilly and Beeson, concerning treatment with sulfonamides and other measures, predominantly penicillin, are also quite favorable.

A predecessor of contemporary antibiotic therapy was the treatment with pyocyanase, based on the research of Freudenreich, Emmerich, and Löw, Gundel and others. Favreuil and Fortiau were able to cure 68 out of 69 cases of anthrax.

One year after the discovery of penicillin, Fleming demonstrated an effect of this remedy on anthrax pathogens. Later investigations by Abraham, Chain, et al. confirmed these observations and determined moreover that there are anthrax strains extraordinarily sensitive to penicillin. In 1944, Murphy,

La Rocatta and Lockwood were the first to describe favorable results in the treatment of humans. This was followed by reports from Ellingson, Rookwalter, and Howe, who cured 25 patients with 1 - 400,000 units, but who pointed out a phenomenon later confirmed by us and others, namely, that carbuncles continue to develop for some time despite the destruction of the pathogens. Griffin and co-workers still combined with sulfonamides in the treatment of 10 patients (100,000 - 300,000 units every 3 hours, up to a total dosage of 13,000,000 on the average), 17 additional cases were treated solely with the antibiotic. They recommend large dosages because they found that certain strains of anthrax are relatively insensitive to penicillin.

The therapeutic approach in penicillin therapy is variable. A few writers, e.g. Stott (1 case), LaRocetta (36 cases), Weinstein and Oliver (3 cases) dispense the drug only intramuscularly. Abraham injected a total of 600,000 units into the anthracic focus. Vidals and Scodeller instilled 40,000 units around the pustule and 60,000 under the pustule. Weinstein, together with Harris, still recommended infiltration therapy alone as late as 1945. Additional favorable results with intramuscular treatment, partly with combined management, are reported by Brunner, Mitchell-Heggs, Reque, Noguer-More. Gruenigar uses local compresses with penicillin and simultaneously prescribes intravenous drip therapy with daily doses of 100,000 - 200,000 units, for a total treatment with 500,000 - 800,000 units. Kolmer, who dispenses 20,000 - 40,000 units every 3 hours, recommends a blood culture in every severe case, and, upon a positive demonstration as well as in all cases of pulmonary and intestinal anthrax, continuation of penicillin in dosages of 200,000 - 300,000 units until the blood cultures become negative.

Reilly and Beeson treated 4 cases with combination therapy using 300,000 units and 6 grams sulfadiazine daily for 5 days. One patient was successfully managed with 2 grams streptomycin daily. Lebrun succeeded in saving a case with a combination of penicillin and sulfonamide which had advanced from a pustula maligna on the upper lip to thrombophlebitis. Shanahan's success in the combined treatment of anthrax meningitis has already been pointed out.

Despite the positive evaluation of penicillin therapy, certain factors must nevertheless be made clear: 1. The development of the pustular stage is not altered as already pointed out. Although further dissemination is prevented (Ellingson and co-workers, Gold, Mohr and others). 2. The positive demonstration may, in some cases, outlast the beginning of the clinical recovery (Gold). Mohr noted this particularly in connection with those anthrax strains that grew with a marked hemolytic zone on blood agar plates. Mann points out the necessity for constant bacteriological surveillance due to the circumstance that anthrax bacilli occasionally produce penicillinase, rendering the results questionable. Generally speaking, the bacilli are no longer culturally demonstrable within 24 hours, as determined by Ellingson and co-workers in 25 cases (they dispensed 1 - 4 million units intramuscularly in most cases, locally in others).

Penicillin therapy is not wholly accepted by Robert, who attributes only secondary importance to it and gives pre-eminence to biological methods of treatment.

Personal experiance with a total of 13 cases has led us to adopt a combined therapy resembling that of Marchionini. We inject 200,000 units around and under the focus on the first day of treatment; if the focus appears malignant, this process is repeated on the 2nd day, under unusual conditions even on the 3rd. In addition, we prescribe 300,000 - 400,000 units of penicillin suspension intramuscularly over 6 or a maximum of 7 days. After 2 days of treatment in this manner, the pathogen is no longer demonstrable in the wound secretion. We saw two exceptions in the case of hemolytic strains that were shown culturally on the 3rd and 4th day of treatment, respectively, although native preparations were negative. Serum was instilled only in one particularly serious case.

As an example of the efficacy of penicillin therapy in such a serious condition, the following clinical record is reproduced in abbreviated form.

A. Z., a 53-year-old man in good general health. Employed as stevedore in the harbor, occupied with the unloading of skins several days ago. Noticed a small spot on the left upper arm since 2 - 3 days ago. A pustule appeared, followed by a scab. On the day of admission to the hospital, the pustule had been slightly forced for the purpose of obtaining the secretion, and the scab had been removed. At the time of admission, the lesion presented as in Fig. 3. Treatment was immediately commenced by subpustular injection of 200,000 units and instillation of 300,000 units of penicillin suspension. Nevertheless, rigor set in during the evening, the swelling on the arm increased during the night, the temperature rose and the clinical picture took on an extremely septic aspect.

Under these conditions penicillin dosage was increased and the antibiotic was injected in doses of 50,000 units every 2 hours. In addition, the patient received 20 cm^3 serum. This condition improved rapidly under regular penicillin treatment every 2 - 3 hours and daily dosages of 600,000 to 800,000 units, even though the local lesion behaved as indicated and restitution was quite slow.

The strain was frankly hemolytic and was demonstrable in the culture up to the 3rd day of illness in spite of very intense treatment.

It must be emphasized in a critical evaluation of this case in particular, that the temperature elevation continued and the situation worsened despite local and intramuscular application of penicillin. This circumstance seems to indicate that serum therapy should not be abandoned entirely, notwithstanding the negative results of animal experiments by McCullough and V. Auersperg, and that it should be resorted to in serious cases as before. On such occasions, 40 and 50 cm^3 serum may be dispensed without hesitation for 2 or 3 days. It is recommended, in this connection, to instil part of the serum intravenously, say 20 cm^3 intravenously and 30 cm^3 intramuscularly on the first day, the same dosage or a reduced one on the second day, i. e. about 10 cm^3 intravenously and 20 cm^3 intramuscularly, while the dose on the 3rd day would conform to the situation, being either unchanged or reduced farther. A second factor should be pointed out: Reservations have been voiced from various quarters regarding local application of penicillin in the form of infiltration. The aforementioned case, especially, compelled us to subject our opinion concerning peripustular and subpustular injection to a certain revision, so that we proceed more cautiously in the case of localization in the face, especially the eyelids,

cheeks and chin, while local application is retained in connection with all other localizations. Care must be taken not to upset the normal conditions of humal saturation by excessive fluid infiltration, since otherwise the penicillin injected intramuscularly, which is transported by the circulation, will not reach its destination.

The most recent American methods of anthrax therapy dispense with serum and make exclusive use of penicillin (Keefer). They consider a daily intramuscular dose of 100,000 - 200,000 units sufficient and prescribe it for 3 - 7 days, depending on the patient's reaction.

This type of therapy makes extensive local measures unnecessary. A protective dressing with penicillin salve or, preferably a penicillin-saturated compress, together with strict immobilization of the affected limb, is quite satisfactory. It is understood that the anthracic patient must observe strict bedrest during the first few days.

In the case of pulmonary anthrax and intestinal anthrax, as well as anthracic sepsis, the employment of penicillin, serum and, if necessary, sulfonamide combinations, is naturally indicated in order to prevent what otherwise would be disaster.

Prophylaxis. Human infections invariably are traced back to infected animal products. For this reason, prevention consists essentially of the control of anthrax among animals. This is carried out in all civilized countries on a legal basis. Anthrax is reportable. The principal task is to identify all animals that have been infected with anthrax or have died of the disease, and to eliminate them together with their excretion. The government therefore compensates for all animal losses due to anthrax, even in cases where the report was overdue. In peracutely developing cases the owner does not even have a chance to report the infection in time. Attempts to cure anthracic animals may be undertaken only by veterinarians. Stalls of diseased and affected animals must be isolated and subjected to intense disinfection at once. Cadavers must be transported to animal processing plants in tightly closed vehicles. Dissection and skinning outside flaying establishments is prohibited. Cadavers must be eliminated by burning or by technical processing. The latter is accomplished by boiling until the soft parts disintegrate or by dry distillation. In Germany, the burial of anthracic cadavers is forbidden. Since a complete, harmless elimination of anthracic cadavers is difficult in uncivilized countries and, especially, in the steppes, this explains the high prevalence of anthrax in these countries. Losses in livestock are here prevented by immunization with attenuated anthrax bacilli or spores, which affords positive protection for one year. In many parts of South America, Africa and Asia, profitable animal husbandry would be impossible without the annual vaccination due to the high incidence of anthrax.

A number of ordinances have been issued to prevent the importation of anthrax bacilli in foreign animal products. Meat and bone meal must be sterilized prior to importation. Imported animal hairs and bristles must be disinfected by steam with addition of 10% formaldehyde; wool by washing in soapy water at 39 - 43°C and subsequent soaking in 2% formaldehyde or flowing steam

at 0.15 atmospheric pressure. Sterilization of hides is difficult, since the tanning properties must not be impaired. One therefore attempts to identify infected skins prior to tanning. This is done by preparing a cold extract of punched-out samples, which then is subjected to precipitation. The inactivation of tannery sewage is very difficult since chemical disinfection of the wastes cannot be carried out. Devitalization of anthrax bacilli is guaranteed only in the solid tailing of tanneries brought about by composting for 3 months with addition of quicklime. Safety regulations have been issued in enterprises that may conceivably handle anthracic material, e.g. the leather and brush industries. Maritime transport workers must be equipped with head and neck guards during the transport of skins.

Prophylactic vaccination of humans, which incorporates grave dangers, must be actively discouraged.

Experience gained in Hamburg's industries indicates that appropriate education leads to early treatment of diseased persons. The prognosis is considerably improved thereby and the duration of illness shortened. However, the necessity for the reporting and isolation of every case of human anthrax remains unchanged, since it is inadvisable to keep the patient in his domestic milieu, despite the improved therapeutic methods currently in use. The dressings of cutaneous lesions, the sputum of pulmonary patients and the feces and urine, particularly in the case of intestinal anthrax, must be disinfected.

Pseudoanthrax

Various difficulties exist in connection with this disorder. Whether it is to be classed with the zoonoses and whether in clinical relation of pseudoanthrax to anthrax corresponds to the relationship between paratyphus and typhus, remains to be solved by further thoroughgoing investigation, as stressed by Wilamowski and Poppe.

The variability to B. anthracis was observed at the Institute Pasteur as early as 1883. In addition to small deviations from the classic type, various pseudo-strains have been grown that differ radically from B. anthracis. These are motile, strongly hemopeptic even in young cultures, and grow in broth with initial turbidity and subsequent clearing with sediment and membrane formation. Some of these strains are described as apathogenic (Poppe, Wagner). Koehler claimed to be able to use the mouse test in differentiation (pseudostrains are said to be pathogenic only for mice, and not for larger animals or man). This is contrasted with Schuermann's report of death resulting from a case of human pseudoanthrax.

Several authors believe the distinct hemolysis in young, 16-hour cultures on blood agar to be one of the most important criteria of pseudo-strains. Lippelt, on the other hand, noted hemolysis in two clinically very serious cases of anthrax, in the presence of all other signs of B. anthracis.

Ascoli's thermoprecipitation similarly cannot be considered a positive differential-diagnostic measure, since Pasteur vaccines and pseudo-strains frequently cause greater precipitation than B. anthracis.

The thermal resistance of pseudoanthrax bacilli usually is greater than that of the genuine anthrax pathogen.

The differentiation of B. anthracis or pseudoanthracis requires a careful examination of the germs for their variable properties by various methods (Gillissen and List).

The clinical picture of a pseudoanthrax infection essentially resembles that of anthracic sepsis (Poppe) with severe generalized manifestations, heavy local edema, diarrhea, swellings of the liver and spleen. The diagnosis was ascertained post mortem in most cases. Autopsy revealed pulmonary edema, hemorrhagic pleuritis, splenic tumor, swelling of the liver, and meningitis.

This clinical appearance corresponds approximately to severe anthracic sepsis.

The literature to date contains no data on the efficacy of anthrax serum in pseudoanthracic disorders or on penicillin therapy of such infections.

Illustrations

Fig. 1 Anthrax bacilli in a lesion smear.

Fig. 2 Anthrax carbuncle on the cheek with a central papillary scab and surrounding erythema.

Fig. 3 Anthrax carbuncle on the elbow with a central eschar of blackish color and vesiculation in the peripheral zones.

Fig. 4 Anthrax carbuncle on the forehead with accompanying edema of the upper lip.

Fig. 5 Anthrax carbuncle on the cheek, 3rd day of illness prior to commencement of penicillin therapy.

Fig. 6 The same carbuncle after penicillin treatment 6 days later.

Fig. 7 Anthrax carbuncle on the elbow, see Fig. 3, with septic distribution and favorable restitution under intense penicillin therapy.

Fig. 8 Anthrax carbuncle on the throat, good recovery under penicillin therapy. Conspicuously long persistence of anthrax bacilli, growing with a hemolytic zone, but otherwise revealing all signs of the typical anthrax bacillus (Lippelt).

Vol. I, pp. 1267-1270

(From W. Volland: Lesions of the Central Nervous System Caused by Infectious Diseases.)

9. Anthrax

Anthrax, an acute infectious disease occurring as a pronounced occupational illness and becoming progressively rarer in Germany and in many other civilized countries, is accompanied by high-grade bacteremia and general hemorrhagic diathesis. These two characteristics are important for the pathogenesis of pathologic-anatomical lesions of the central nervous system, demonstrable at a high percent rate in connection with anthrax.

Hemorrhagic anthracic meningitis, first described in 1874 by Wagner, is so characteristic that it could almost be called specific; for whereas the liquor is usually free of blood in meningitides of every genesis, it regularly contains blood in anthracic meningitis (Lusthy). Macroscopically, the serous-hemorrhagic or frankly hemorrhagic meningeal exudate which prefers the convexity of the brain, is seen in pronounced cases as a layer of blood up to 1 cm in thickness, covering the cerebral surface in the form of a hood (Pette, Weimann and others). However, spotty hemorrhages in the region of the soft membranes have also been observed (Silberberg, Martinoff). Microscopically there are frequently considerable amounts of white blood cells, such as leucocytes, lymphocytes and macrophages (Wohlwill, Weimann), in the region of the arachnoidal network, in addition to erythrocytes and fibrin, justifying Moore's description of "sanguinopurulent leptomeningitis" in connection with anthrax. In view of the pronounced hemorrhagic nature of the inflammation, the vascular lesions are noteworthy which, demonstrated as early as 1886 by Marchand and said by Herzog to be present as a rule, are marked by severe regressive wall defects, especially in the region of the media, including necrosis. Degeneration of muscular fibers predominates. Laceration of the elastica leads to appearances recalling dissected aneurysms. According to Herzog, the hemal extravasates develop either per diapedesis or (by laceration of the adventitia) per rhexis. While Herzog ascribes major responsibility for the occurrence of hemorrhages to the arteries, Bezi, who does not deny the reality of massive hemorrhages on the base of circumscribed wall necroses of small and medium-sized arteries, considers the veins particularly vulnerable owing to their weaker walls and, in contrast to Herzog, places the inception of the process in the outer layers of the wall. The perivascular arrangement of pathogens in anthracic meningitis described by Wagner in 1874 and by numerous investigators after him, represents a finding in support of this concept. The anthrax bacilli which may be grown from sanguinolent liquor (Pette), may also be demonstrated in histological sections, at times in enormous amounts. Frequently they are more copious in the hemorrhagic exudate than in the lumina of the meningeal and cerebral vessels (Paltauf). Yet, they have been encountered even here at times, occasionally in large amounts, especially in connection with leptomeningitis anthracica of hematogenic - metastatic genesis (Merkel, Nieberle).

While Bezi (1926) estimates that 40% of all fatal cases of human anthrax infection reveal meningeal or intracerebral hemorrhages, Poppe lists the total

mortality of human anthrax at 10-20%. According to this author, the lethality of internal anthrax approaches 100%, that of external anthrax fluctuates between 5 and 35%. Sobernheim claims a variation in anthracic mortality based on location and time. Thus, for instance, England reported 714 cases during the years 1910-1920, of which 106, i.e. 14.8%, died. In France, there were 405 reported cases during the same period with 49, i.e. 12.07% fatal terminations, while 1,175 cases were reported in Germany during the period 1911-1919, of which 16.11% were lethal. Since anthrax is an occupational disease of workers dealing with foreign hides, animal hair and bristles, infections among children are extraordinarily rare. Eck described a case of anthracic meningitis involving a 1-year-old girl. The primary focus was located in the nasal mucous membrane. A toy stuffed with hairs and rags containing anthrax spores was identified as the source of infection. A placental anthrax infection observed by Marchand also involved the central nervous system. Whereas heretofore anthrax had been treated principally with anthrax serum, salvarsan and sulfonamides (Poppe), modern penicillin therapy ought to lead to a considerably more favorable prognosis in anthrax.

The soft spinal cord membranes may be affected by hemorrhagic anthracic meningitis in the same manner as the meninges (Petta, Nieberle). From here, the inflammatory process occasionally invades the spinal cord proper in the form of meningomyelitis (Fedechtal). Hanse observed a case of anthrax-induced meningo-encephalomyelitis which had presented an encephalomyelitic picture recalling multiple sclerosis after the abatement of the acute manifestations. Onorato also describes a spinal symptomatology after infection with anthrax, followed by restoration of health.

Frequently, but not invariably, hemorrhagic anthrax meningitis is accompanied by punctiform cerebral hemorrhages localized perivascularly in the cerebral cortex and also in the basal ganglia and the medullary layer. Histologically, these involve predominantly pure hemorrhages (Pette), whereas the hemorrhagic exudate of the soft membranes usually contains copious leucocytes, as already stressed. On the other hand, leucocytes may also be well represented intracerebrally in addition to erythrocytes, justifying Wohlwill and Weimann's designation "hemorrhagic encephalitis". The accompanying injury to the neural parenchyma generally is relatively mild, although nerve swellings and liquefaction as well as regressive changes in the glia, e.g. amoboid transformation of the glia, may occur (Fuchi, Weimann).

As in leptomeningitides of different etiology, the dissemination of anthrax pathogens in the soft meninges also takes place either by lymphogenic drainage from the surroundings (Ziemke and others) or metastatically through the blood circulation (Nieberle and others), and this happens so frequently in fatal cases that a certain affinity of anthrax bacilli for the meninges has been suggested (Adelheim and Kuktin), especially since Bexi refers to the demonstration of meningeal or intracerebral hemorrhages in 40% of all fatal cases of anthrax. Bemmoldt-Thomsen's 6 cases of hemorrhagic anthrax meningitis involved two instances of inhalation anthrax, while the remaining 4 cases revealed portals of entry on the tongue near the cranial cavity, on the cheek, the upper lip, and the skin of the neck. It is obvious that the hemorrhagic character of anthracic meningitis is tied to the general hemorrhagenic tendency of this infectious disease. Its principal cause indubitably is based on damage

to the vascular wall which is expressed histologically by necrosis of the media and its sequels. Personal studies of anthracic guinea pigs carried out with the collaboration of Arnolds and Brede demonstrated a positive Rumpel-Leede phenomenon in support of the "vascular factor," which certainly dominated the cause of bleeding in these cases. In addition, the bleeding time, the coagulation time and the prothrombin time were prolonged and the number of platelets diminished. Thus it was confirmed again that disorders of the hemostatic reaction are never caused by dysfunction of a single hemostatic factor. Rather, according to Jurgens, several factors are invariably involved, of which the dominating one -- in this case, the vascular factor -- frequently determines the type of hemorrhagic diathesis.

Concerning the question, in which manner the pathogens attack the vascular wall, it must be emphasized that the existence of anthracic toxins has not been disproved conclusively, nor has it been verified (Lommel, Sobernheim and others). The hypothesis first defended by Toussaint and discussed by Lommel as late as 1934, according to which the hemorrhages owe their genesis to bacterial embolism in the sense of hemorrhagic infarction, in view of the occurrence of occasionally quite massive bacteremia, cannot withstand the criticism of the histopathologist; for, aside from the fact that the predominantly meningeal hemorrhages in no way present the picture of air or fat embolism of the brain, the changes in the nerve cells (which sometimes are relatively mild) tend to contradict this concept. On the other hand, it seems important to us that anthrax bacilli have been demonstrated to possess proteolytic faculties (literature in H. Schmidt). The massive dissemination of pathogens consequently explains the histiolytic effect on vascular walls, after Baerthlein had described the "hemopeptic" influence of an anthracic strain in 1914, i.e. the capability to degrade erythrocytes, including their stroma.

Although anthrax bacilli are also pathogenic for our domestic animals (plant eaters and swine) as well as for rodents used as laboratory animals, and also evoke a septicemic picture accompanied by bacteremia, splenic swelling and hemorrhagic diathesis, hemorrhagic anthracic meningitis does not play the same role among animals as it does in human pathology. Although Nieberle (1925/26) fails to find references to animal leptomeningitis anthracica in the literature, he does not doubt the occurrence of hemorrhagic anthrax meningitis among animals on the basis of reports of capillary bleeding and spotty hemal coagula between the meninges; nevertheless, it is undoubtedly rare. The main reason for this divergence from human pathology apparently is the high incidence of internal anthrax, especially the intestinal type, among domestic animals, whereas human afflictions are dominated at the rate of 28-40% by cutaneous anthrax localized on the head, throat or neck, i.e. on unprotected parts, from which a lymphogenic dissemination toward the neighboring cranial cavity is easily possible (Poppe). In view of the fact that human hemorrhagic anthrax meningitis may also develop hematogenically from a primary focus in the region of the digestive tract (Risel) or by inhalation (Kreisel, Poelschau, Drodzda), it should be stressed that hematogenic cerebral metastases and cerebral emboli are rare in animals when compared to man, primarily because the small size of animal brains in comparison to the remaining parts of the head requires a different distribution of arterial blood than that found in man and, consequently, a different distribution of introduced emboli (Joest). Moreover, inhalation anthrax may also induce a primary focus in the nasal region, so

that this mode of infection could also cause meningitis through lymphogenic dissemination of pathogens.

Finally, mention should be made of anthrax as one of these infectious diseases that may be followed by pachymeningitis (pachymeningosis) hemorrhagica interna (Fette). Still, the positive delineation of this disorder of the dura mater against the subdural hemorrhages associated with anthrax, where these occur only as a symptom of general hemorrhagic diathesis, will be difficult in some cases.

Vol. IV, pp. 359-360

Anthracic meningitis (meningitis anthracica)

(From H. Petre: Pachymeningitis and leptomeningitis.)

Anthracic meningitis is an inflammatory disorder of the soft cerebral and spinal cord membranes characterized by very extensive hemorrhages within the arachnoidal spaces. The hemorrhagic inflammation, which may lead to profuse spotty bleeding, is localized predominantly in the cerebral convexity and in very severe cases resembles a red hood superimposed on the brain.

The first case of anthracic meningitis was reported by Wagner in 1874. This was followed by additional cases presented by Paltauf, Marchand, Merkel, Goldschmidt, E. Fraenkel. In 1913 Fr. Fulci collected the material, scattered throughout the literature, into a comprehensive paper and added a very thoroughly studied case of his own.

Wohlwill found in the cases studied by him that red and white hemal elements were represented in equal parts in the region of the inflammatory meningeal lesions. The situation was different in the cerebral substance, where pure hemorrhages generally predominated; these do not occur in the manner of annular hemorrhages, but fill the strongly dilated lymph sheaths under considerable pressure. Since the main concentrations of parenchymal lesions are located in the cortex, the basal ganglia and the medullary layer, it must be assumed with Wohlwill and other authors that the pathogens enter the brain by the lymphatic route.

Marchand determined as early as 1885 that the entire vascular wall may disintegrate due to necrosis and purulent inflammation. Necrosis is probably caused by the toxins of anthrax bacilli located in massive proportions in the soft membranes. Herzog considered the extensive meningeal hemorrhages a sequel to a severe disorder of the vascular media. Identical investigations led Bezi to the conclusion that profuse bleeding in the meningeal region sets in only when anthrax bacilli have undergone massive reproduction in the vascular lymph sheaths and the lymph spaces of the membranes.

Meningitis is so frequently seen in fatal cases of anthrax that Adelheim and Kaktin assume a certain affinity of the anthrax bacillus for the meninges.

Briefly noted, the pathogen of anthrax may enter the organism and, consequently, the meninges by various routes: 1. by penetration from small cutaneous wounds, 2. by swallowing (intestinal anthrax), and 3. by inhalation (pulmonary anthrax). Of these forms, cutaneous anthrax is most prevalent.

The clinical picture of anthracic meningitis agrees with the anatomical situation, provided the manifestations of meningeal irritation based on diffuse meningeal bleeding develop within a short period of time and soon lead to death under deep disturbances of consciousness.

However, death in these cases may also occur quite suddenly, as was noted in a patient observed by Herzog. He complained of malaise while walking around and died within one hour under tonic-clonic cramps. Another case, described by Kaye, was not quite as stormy. The 59-year-old man, who had complained of malaise, nausea and weakness in the legs the day before, had risen in the morning. He became confused in the afternoon, comatose in the evening, and died a few hours later.

Hauss has reported a peculiar case of anthracic meningo-myeloencephalitis. In the wake of a malignant carbuncle on the forearm, the 39-year-old man developed the picture of meningitis with high-grade somnolence and deliriant agitation. After the abatement of acute manifestations, encephalomyelitic symptoms developed which strongly resembled the picture of multiple sclerosis.

The liquor is sanguinolent in pronounced cases of anthracic meningitis. It yields pure cultures of anthrax bacilli regularly and with ease, facilitating the diagnosis of anthracic meningitis upon positive findings in the liquor.

E. Fraenkel considers the bacteriological examination of lumbar punctate absolutely necessary in every case of anthrax.

Vol. IV, pp. 806-808

4. Anthracic pneumonia

(From A. Lauche: Inflammations of the lung and pleura)

An anthracic infection of the lung has great similarity to the picture of pulmonary plague. In the case of anthrax we must also differentiate between an infection via the skin (pustula maligna) and inhalation anthrax (E. Fraenkel, Nieberle). We are concerned primarily with inhalation anthrax, "woolsorter's" or "rag" disease (Paltauf, Eppinger). E.Fraenkel emphasizes in his recently published paper on inhalation anthrax that the primary infection frequently takes place in the bronchial mucous membrane, preferably at the point of bifurcation. From here it wanders to the glands of the hilus and evokes in these an hemorrhagic-necrotizing inflammation quite similar to that associated with the foci of plague. The pulmonary tissue proper is not necessarily attacked at the start. For this reason E. Fraenkel speaks of inhalation anthrax and not of pulmonary anthrax. Pulmonary anthrax is involved only when pneumonic foci are actually present in the lung, which is frequently, but not invariably, the case in inhalation anthrax. According to E. Fraenkel, the pneumonic foci in the lungs develop by aspiration from the primary bronchial foci, and only rarely by the hemal or lymphatic route in the manner accepted heretofore.

The anatomical picture of anthracic pneumonia is very similar to the findings in pneumonic plague. Anthracic foci are also marked by a tendency to hemorrhages and disintegration (Eppinger, Paltauf). As in pneumonic plague, the hilus glands are greatly swollen and show hemorrhagic-necrotizing inflammation (E. Fraenkel). This conspicuous involvement of the lymph glands will first suggest an anthracic disease during section. In addition, serous or hemorrhagic pleuritis is present in many instances.

The histological appearance of anthrax pneumonia also resembles pneumonic plague very closely, with the exception that numerous anthrax bacilli are found instead of plague bacilli, even though in smaller numbers. They are particularly well representable and distinct with Weigert's fibrin stain (Fig. 36). The exudate contains copious fibrin more frequently than in pneumonic plague. According to E. Fraenkel and Reye, the anthrax bacilli are capable of inducing "croupous" inflammations in the bronchi that are analogous to the pseudo-membranes of diphtheria. In the pneumonic anthrax material made available to me by Professor Fraenkel, the fibrinous exudate predominates in many foci. Other foci are cellular; no hemorrhagic areas were seen. Although the material was difficult to stain, probably due to late fixation after death (the rapid putrefaction of anthracic corpses is well known, Paltauf, Sobernheim), the anthrax bacilli were favorably depicted. They were found in copious quantities both in the alveolar walls and the fibrinous masses of exudate. I was unable to determine the extent to which a post-mortal reproduction was involved, since no fresh material was available to me owing to Professor Fraenkel's death in the meantime, and none could be obtained from other sources. Cases of anthrax, especially inhalation anthrax, have become rarer in Germany and there will be few opportunities for differential-diagnostic considerations in order to arrive at an identification

of anthrax, plague or influenza during dissection with a modicum of probability.

Under no circumstances can a positive diagnosis be made from the macroscopic appearance, since all three diseases may be marked by hemorrhagic and necrotizing inflammatory processes; all three are also accompanied by severe swelling and frequently hemorrhagic inflammation of the bronchial glands. Moreover, Kuczynski and Wolff state that the degenerative forms of streptococci, often found in influenza, are extraordinarily similar to the involution forms of the plague bacillus. This is valid also for anthrax bacilli (see Fig. 36). These may also develop club-shaped and irregular rods. The microscopic examination of the pulmonary tissue proper will permit a decision in most cases, since a large number of pathogens usually are still well preserved and allow an identification even by bacterioscopic means. Some cases, however, may yield final clarification only through the animal test. Concerning the difficulties encountered in differential diagnosis between anthrax, plague and influenzal pneumonia on one hand, and war gas pneumonias on the other, I refer the reader to the description of war gas pneumonias (p. 817).